

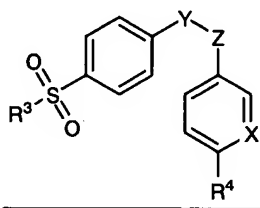
### **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims:**

Claim 1 (currently amended): An orally deliverable pharmaceutical composition comprising

(a) a selective cyclooxygenase-2 inhibitory drug of low water solubility **having the formula**



**where R<sup>3</sup> is a methyl or amino group, R<sup>4</sup> is hydrogen or a C<sub>1-4</sub> alkyl or alkoxy group, X is N or CR<sup>5</sup> where R<sup>5</sup> is hydrogen or halogen, and Y and Z are independently carbon or nitrogen atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups; or a prodrug of such a compound;**

(b) a pharmaceutically acceptable solvent liquid **selected from the group consisting of glycols and glycol ethers;** and

(c) a turbidity-decreasing polymer;

wherein at least a substantial portion of the drug is in dissolved or solubilized form in the solvent liquid, and wherein said polymer is present in an amount sufficient to substantially inhibit crystallization and/or precipitation of the drug in simulated gastric fluid.

Claim 2 (original): The composition of Claim 1 wherein the drug is present in a therapeutically effective amount.

Claim 3 (original): The composition of Claim 1 wherein the drug is present in a total amount of about 1% to about 75% by weight of the composition.

Claim 4 (original): The composition of Claim 1 wherein at least about 15% of the drug is present in the solvent liquid in dissolved or solubilized form.

Claim 5 (original): The composition of Claim 1 wherein substantially all of the drug is present in the solvent liquid in dissolved or solubilized form.

Claims 6-7 (cancelled).

Claim 8 (currently amended): The composition of Claim 1 **[[7]]** wherein the five- to six-membered ring is selected from cyclopentenone, furanone, methylpyrazole, isoxazole and pyridine rings substituted at no more than one position.

Claim 9 (currently amended): The composition of Claim 1 **[[6]]** wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one, (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.

Claim 10 (original): The composition of Claim 9 wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib.

Claim 11 (original): The composition of Claim 10 that comprises one or more dose units each comprising about 10 mg to about 1000 mg of celecoxib.

Claim 12 (original): The composition of Claim 10 that comprises one or more dose units each comprising about 50 mg to about 400 mg of celecoxib.

Claim 13 (original): The composition of Claim 9 wherein the drug is valdecoxib.

Claim 14 (original): The composition of Claim 1 wherein the turbidity-decreasing polymer is selected from the group consisting of polyvinylpyrrolidone and cellulosic polymers.

Claim 15 (original): The composition of Claim 1 wherein the turbidity-decreasing polymer is a cellulosic polymer selected from the group consisting of sodium carboxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, hydroxypropylcellulose and ethylcellulose.

Claim 16 (original): The composition of Claim 15 wherein the cellulosic polymer is hydroxypropylmethylcellulose.

Claim 17 (original): The composition of Claim 16 wherein the hydroxypropylmethylcellulose has about 15% to about 35% methoxyl substitution and about 3% to about 15% hydroxypropoxyl substitution.

Claim 18 (previously presented): The composition of Claim 16 wherein the hydroxypropylmethylcellulose has about 19% to about 30% methoxyl substitution and about 4% to about 12% hydroxypropoxyl substitution.

Claim 19 (previously presented): The composition of Claim 16 wherein the hydroxypropylmethylcellulose has about 19% to about 24% methoxyl substitution and about 7% to about 12% hydroxypropoxyl substitution.

Claim 20 (currently amended): The composition of Claim 1 ~~[[6]]~~ further comprising a vasomodulator, wherein the selective cyclooxygenase-2 inhibitory drug and the vasomodulator are present in total and relative amounts effective to relieve pain in headache or migraine.

Claim 21 (currently amended): The composition of Claim 1 ~~[[6]]~~ further comprising an alkylxanthine compound, wherein the selective cyclooxygenase-2 inhibitory drug and the alkylxanthine compound are present in total and relative amounts effective to relieve pain in headache or migraine.

Claim 22 (previously presented): The composition of Claim 21 where in the alkylxanthine compound is selected from the group consisting of caffeine, theophylline and theobromine.

Claim 23 (previously presented): The composition of Claim 21 wherein the alkylxanthine compound is caffeine.

Claim 24 (previously presented): The composition of Claim 1 wherein the turbidity-decreasing polymer is present in the solvent liquid in an amount of about 1% to about 20% by weight of the solvent liquid.

Claim 25 (previously presented): The composition of Claim 1 wherein the turbidity-decreasing polymer is present in the solvent liquid in an amount of about 1% to about 15% by weight of the solvent liquid.

Claim 26 (previously presented): The composition of Claim 1 that is an imbibable liquid.

Claim 27 (previously presented): The composition of Claim 1 further comprising a water-soluble capsule wall wherein the drug and solvent liquid are encapsulated.

Claim 28 (previously presented): The composition of Claim 27 wherein the turbidity-decreasing polymer is present in the capsule wall in an amount of about 5% to about 100% by weight of the wall.

Claim 29 (previously presented): The composition of Claim 27 wherein the turbidity-decreasing polymer is present in the capsule wall in an amount of about 15% to about 100% by weight of the wall.

Claim 30 (cancelled).

Claim 31 (currently amended): The composition of Claim 1 **[[30]]** wherein the solvent is polyethylene glycol.

Claim 32 (currently amended): The composition of Claim 31 **[[30]]** wherein the polyethylene glycol has an average molecular weight of about 100 to about 10,000.

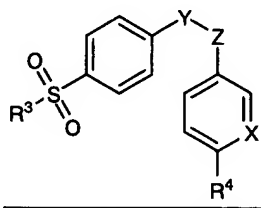
Claim 33 (currently amended): The composition of Claim 31 **[[30]]** wherein the polyethylene glycol has an average molecular weight of about 100 to about 1,000.

Claim 34 (currently amended): The composition of Claim 31 **[[30]]** wherein the polyethylene glycol has an average molecular weight of about 375 to about 450.

Claim 35 (currently amended): The composition of Claim **31** **[[30]]** wherein the polyethylene glycol is of liquid grade.

Claim 36 (currently amended): An orally deliverable pharmaceutical composition comprising

(a) a **selective cyclooxygenase-2 inhibitory** drug of low water solubility **having the formula**



**where R<sup>3</sup> is a methyl or amino group, R<sup>4</sup> is hydrogen or a C<sub>1-4</sub> alkyl or alkoxy group, X is N or CR<sup>5</sup> where R<sup>5</sup> is hydrogen or halogen, and Y and Z are independently carbon or nitrogen atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups; or a prodrug of such a compound;**

(b) a pharmaceutically acceptable solvent liquid **selected from the group consisting of glycols and glycol ethers;** and

(c) a cellulosic polymer;

wherein at least a substantial portion of the drug is in dissolved or solubilized form in the solvent liquid, and wherein said cellulosic polymer is present in an amount sufficient to substantially inhibit crystallization and/or precipitation of the drug in simulated gastric fluid.

Claim 37 (previously presented): The composition of Claim 36 wherein the drug is present in a therapeutically effective amount.

Claim 38 (previously presented): The composition of Claim 36 wherein the drug is present in a total amount of about 1% to about 75% by weight of the composition.

Claim 39 (previously presented): The composition of Claim 36 wherein at least about 15% of the drug is present in the solvent liquid in dissolved or solubilized form.

Claim 40 (previously presented): The composition of Claim 36 wherein substantially all of the drug is present in the solvent liquid in dissolved or solubilized form.

Claims 41-42 (cancelled).

Claim 43 (currently amended): The composition of Claim 36 ~~[[42]]~~ wherein the five- to six-membered ring is selected from cyclopentenone, furanone, methylpyrazole, isoxazole and pyridine rings substituted at no more than one position.

Claim 44 (currently amended): The composition of Claim 36 ~~[[41]]~~ wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one, (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.

Claim 45 (previously presented): The composition of Claim 44 wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib.

Claim 46 (previously presented): The composition of Claim 45 that comprises one or more dose units each comprising about 10 mg to about 1000 mg of celecoxib.

Claim 47 (previously presented): The composition of Claim 45 that comprises one or more dose units each comprising about 50 mg to about 400 mg of celecoxib.

Claim 48 (previously presented): The composition of Claim 43 wherein the drug is valdecoxib.

Claim 49 (previously presented): The composition of Claim 36 wherein the cellulosic polymer is selected from the group consisting of sodium carboxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, hydroxypropylcellulose, and ethylcellulose.

Claim 50 (previously presented): The composition of Claim 36 wherein the cellulosic polymer is hydroxypropylmethylcellulose.

Claim 51 (previously presented): The composition of Claim 50 wherein the hydroxypropylmethylcellulose has about 15% to about 35% methoxyl substitution and about 3% to about 15% hydroxypropoxyl substitution.

Claim 52 (previously presented): The composition of Claim 50 wherein the hydroxypropylmethylcellulose has about 19% to about 30% methoxyl substitution and about 4% to about 12% hydroxypropoxyl substitution.

Claim 53 (previously presented): The composition of Claim 50 wherein the hydroxypropylmethylcellulose has about 19% to about 24% methoxyl substitution and about 7% to about 12% hydroxypropoxyl substitution.

Claim 54 (currently amended): The composition of Claim 36 **[[41]]** further comprising a vasomodulator, wherein the selective cyclooxygenase-2 inhibitory drug and the



vasomodulator are present in total and relative amounts effective to relieve pain in headache or migraine.

Claim 55 (currently amended): The composition of Claim 36 ~~[[41]]~~ further comprising an alkylxanthine compound, wherein the selective cyclooxygenase-2 inhibitory drug and the alkylxanthine compound are present in total and relative amounts effective to relieve pain in headache or migraine.

Claim 56 (previously presented): The composition of Claim 55 wherein the alkylxanthine compound is selected from the group consisting of caffeine, theophylline and theobromine.

Claim 57 (previously presented): The composition of Claim 56 wherein the alkylxanthine compound is caffeine.

Claim 58 (previously presented): The composition of Claim 36 wherein the cellulosic polymer is present in the solvent liquid in an amount of about 1% to about 20% by weight of the solvent liquid.

Claim 59 (previously presented): The composition of Claim 36 wherein the cellulosic polymer is present in the solvent liquid in an amount of about 1% to about 15% by weight of the solvent liquid.

Claim 60 (previously presented): The composition of Claim 36 that is an imbibable liquid.

Claim 61 (previously presented): The composition of Claim 36 further comprising a water-soluble capsule wall wherein the drug and solvent liquid are encapsulated.

Claim 62 (previously presented): The composition of Claim 61 wherein the cellulosic polymer is present in the capsule wall in an amount of about 5% to about 100% by weight of the wall.

Claim 63 (previously presented): The composition of Claim 61 wherein the cellulosic polymer is present in the capsule wall in an amount of about 15% to about 100% by weight of the wall.

Claim 64 (cancelled).

Claim 65 (currently amended): The composition of Claim **36** ~~[[64]]~~ wherein the solvent is polyethylene glycol.

Claim 66 (previously presented): The composition of Claim 65 wherein the polyethylene glycol has an average molecular weight of about 100 to about 10,000.

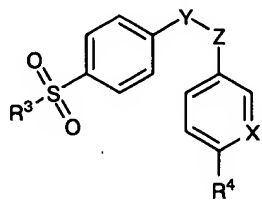
Claim 67 (previously presented): The composition of Claim 65 wherein the polyethylene glycol has an average molecular weight of about 100 to about 1,000.

Claim 68 (previously presented): The composition of Claim 65 wherein the polyethylene glycol has an average molecular weight of about 375 to about 450.

Claim 69 (previously presented): The composition of Claim 65 wherein the polyethylene glycol is of liquid grade.

Claim 70 (currently amended): An orally deliverable pharmaceutical composition comprising a **selective cyclooxygenase-2 inhibitory** drug of low water solubility in a high energy phase together with one or more pharmaceutically acceptable excipients, encapsulated within a capsule wall that comprises a turbidity-decreasing polymer in an

amount effective to substantially inhibit crystallization and/or precipitation of the drug in simulated gastric fluid, **said selective cyclooxygenase-2 inhibitory drug of low water solubility having the formula**



**where R<sup>3</sup> is a methyl or amino group, R<sup>4</sup> is hydrogen or a C<sub>1-4</sub> alkyl or alkoxy group, X is N or CR<sup>5</sup> where R<sup>5</sup> is hydrogen or halogen, and Y and Z are independently carbon or nitrogen atoms defining adjacent atoms of a five- to six-membered ring that is unsubstituted or substituted at one or more positions with oxo, halo, methyl or halomethyl groups; or a prodrug of such a compound.**

Claim 71 (cancelled).

Claim 72 (currently amended): The composition of Claim **70** **[[71]]** wherein the selective cyclooxygenase-2 inhibitory drug is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, 2-(3,5-difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one, (S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid and 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methyl-1-butoxy)-5-[4-(methylsulfonyl)phenyl]-3-(2H)-pyridazinone.

Claim 73 (previously presented): The composition of Claim 72 wherein the selective cyclooxygenase-2 inhibitory drug is celecoxib.

Claim 74 (previously presented): The composition of Claim 70 wherein said high energy phase is an amorphous phase of the drug.

Claim 75 (previously presented): The composition of Claim 70 wherein said high energy phase is a salt of an acid or base form of the drug.

Claim 76 (previously presented): The composition of Claim 70 wherein the turbidity-decreasing polymer is a cellulosic polymer.

Claim 77 (previously presented): The composition of Claim 76 wherein the cellulosic polymer is selected from the group consisting of sodium carboxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, hydroxypropylcellulose, and ethylcellulose.

Claim 78 (previously presented): The composition of Claim 76 wherein the cellulosic polymer is hydroxypropylmethylcellulose.

Claim 79 (previously presented): The composition of Claim 78 wherein the hydroxypropylmethylcellulose has about 15% to about 35% methoxyl substitution and about 3% to about 15% hydroxypropoxyl substitution.

Claim 80 (previously presented): The composition of Claim 78 wherein the hydroxypropylmethylcellulose has about 19% to about 30% methoxyl substitution and about 4% to about 12% hydroxypropoxyl substitution.

Claim 81 (previously presented): The composition of Claim 78 wherein the hydroxypropylmethylcellulose has about 19% to about 24% methoxyl substitution and about 7% to about 12% hydroxypropoxyl substitution.

Claim 82 (previously presented): The composition of Claim 70 wherein the turbidity-decreasing polymer is present in the capsule wall in an amount of about 5% to about 100% by weight of the wall.

Claim 83 (previously presented): The composition of Claim 70 wherein the turbidity-decreasing polymer is present in the capsule wall in an amount of about 15% to about 100% by weight of the wall.

Claim 84 (currently amended): A method of treating a medical condition or disorder in a subject where treatment with a cyclooxygenase-2 inhibitor is indicated, comprising orally administering to the subject a composition of Claim 1 **[[6]]**, Claim 36 **[[41]]**, or Claim 70 **[[71]]**.

Claim 85 (currently amended): A method of analgesia comprising orally administering, to a subject in need of analgesia, an effective pain-relieving amount of a composition of Claim 1 **[[6]]**, Claim 36 **[[41]]**, or Claim 70 **[[71]]**.

Claim 86 (previously presented): The method of Claim 85 wherein the subject suffers from headache or migraine and wherein there is further orally administered to the subject a vasomodulator, the selective cyclooxygenase-2 inhibitory drug and the vasomodulator being administered in total and relative amounts effective to relieve pain in the headache or migraine.

Claim 87 (previously presented): The method of Claim 86 wherein the vasomodulator is co-formulated with the selective cyclooxygenase-2 inhibitory drug.

Claim 88 (previously presented): The method of Claim 85 wherein the subject suffers from headache or migraine and wherein there is further orally administered to the subject an alkylxanthine compound, the selective cyclooxygenase-2 inhibitory drug and the alkylxanthine compound being administered in total and relative amounts effective to relieve pain in the headache or migraine.

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Amendment dated November 23, 2004

Reply to Notice of Non-Compliant Amendment dated November 9, 2004

Claim 89 (previously presented): The method of Claim 88 wherein the alkylxanthine compound is co-formulated with the selective cyclooxygenase-2 inhibitory drug.

Claim 90 (previously presented): The method of Claim 89 wherein the alkylxanthine compound is selected from the group consisting of caffeine, theophylline, and theobromine.

Claim 91 (previously presented): The method of Claim 89 wherein the alkylxanthine compound is caffeine.